REMARKS

Applicants have filed a terminal disclaimer herein over copending application serial number 10/071,248 to eliminate the obviousness type double patenting rejection.

Contrary to the assertions in the office action, applicants submit the terminal disclaimer now on file disclaims any patent term extending beyond the term of US patent No. 7,235,576 B1 **and** any term extending beyond the term of a patent which issues on copending application 09/993,647.

Applicants have expressly abandoned application no. 09/948,915 in favor of a divisional application serial no. 11/845,595, filed August 27, 2007 with claims directed to Group Ia (compounds of formula I where L, L^1 and B are phenyl) and Group Ic (compounds of formula I where L is phenyl and L^1 and B are pyridyl) defined in 09/948,915. Applicants have also expressly abandoned application no. 10/086,417 in favor of a divisional application serial no. 11/845,597, filed August 27, 2007 with method claims directed to define compounds of formula I where either B is not phenyl or L^1 is not pyridyl. Copies of the preliminary amendments made in each divisional application are provided as attachments A and B. The express abandonments of application nos. 09/948,915 and 10/086,417 are provided as attachments C and D.

The compounds defined within the claims of US App. No. 10/086,417 and the divisional application of US App. No. 09/948,915 were subject to a restriction requirement in the present application and not elected. The elected subject matter of this application (modified Group IV), as described in the office action of May 25, 2006, is drawn to compounds of formula I where L^1 is a pyridinyl substituted by at least $C(O)R_x$, L is phenyl and B is phenyl substituted by R^7 and hydrogen.

A rejection for obviousness type double patenting based on the claims within the divisional applications of US App Nos. 09/948,915 and 10/086,417 would be inconsistent with the restriction requirement made in this application. Therefore, applicants submit the obviousness type double patenting rejections based on abandoned US App Nos. 09/948,915 and 10/086,417 should be withdrawn and not renewed for the divisional applications.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Attorney Docket No.: BAYER-0015-A

Date: August 28, 2007

RJT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

RIEDL, Bernd, et. al. Examiner: Delacroix Muirhei, Cybille

Serial No.: Group Art Unit: 1614

Filed: August 27, 2007

Title: OMEGA-CARBOXY ARYL SUBSTITUTED DIPHENYL UREAS AS p38 KINASE INHIBITORS

Preliminary Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Prior to examination, please amend the above-identified application as follows.

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims, which begins on page 3 of this paper.

Remarks/Arguments begin on page 20 of this paper

In the Specification:

Please amend the Specification as follows:

On page 1 the first full paragraph has been amended as following:

~~This is a continuation-in-part of Serial No. 09/257,265 filed February 25, 1999 and a continuation-in-part of Serial No. 60/115,878 filed January 13, 1999.~~

This application is a division of Application No.: 10/086,417, filed March 4, 2002, which is a continuation of Application Number 09/425,229, filed October 22, 1999 which is a continuation-in-part of Application Number 09/257,265 filed February 25, 1999. This application claims the benefit of the filing date of U.S. Provisional Application No. 60/115,878, filed January 13, 1999. The content of these applications are incorporated herein by reference.

This listing of claims will replace all prior versions, and listings, of claims in the application:

Cancel claims 1-38

Claim 39 (New) A method of treating a condition mediated by p38 within a host, said method comprising administering to said host a compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L^1)$_q$, where L is a 5 or 6 membered cyclic structure bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur other than phenyl,

wherein L^1 is substituted by at least one substituent selected from the group consisting of -SO_2R_x, -$C(O)R_x$ and -$C(NR_y)$ R_z,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and

halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R^7)-, -$(CH_2)_m$-, -C(O)-, -CH(OH)-, -$(CH_2)_m$O-, -$(CH_2)_m$S-, -$(CH_2)_m$N(R^7)-, -O$(CH_2)_m$- CHX^a-, -CX^a_2-, -S-$(CH_2)_m$- and -N(R^7)$(CH_2)_m$-, where m= 1-3, and X^a is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO_2R^7, -C(O)R^7, -C(O)NR^7R^7, -NO_2, -OR^7, - SR^7 -NR^7R^7, -NR^7C(O)OR^7, -NR^7C(O)R^7, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO_2R^7, -COR^7, -C(O)NR^7R^7, -OR^7, -SR^7, -NO_2, -NR^7R^7, -NR^7C(O)R^7, and -NR^7C(O)OR^7, with R^7 as defined above.

40. (**New**) A method as in claim 39 for the treatment of a disease other than cancer.

41. (**New**) A method as in claim 39 wherein the condition within a host treated by administering a compound of formula I is rheumatoid arthritis, osteoarthritis, septic arthritis, tumor metastasis, periodontal disease, corneal ulceration, proteinuria, coronary thrombosis from atherosclerotic plaque, aneurysmal aortic, birth control, dystrophobic epidermolysis bullosa, degenerative cartilage loss following traumatic joint injury, osteopenias mediated by MMP activity, tempero mandibular joint disease or demyelating disease of the nervous system.

42. (**New**) A method as in claim 39 wherein M is a bridging group which is one or more groups selected from the group consisting of -O-, -S-, -N(R^7)-, -$(CH_2)_m$-, -C(O)-, -CH(OH)-, -$(CH_2)_m$O-, -$(CH_2)_m$S-, -$(CH_2)_m$N(R^7)-, -O$(CH_2)_m$- CHX^a-, -CX^a_2-, -S-$(CH_2)_m$- or ~~and~~ -N(R^7)$(CH_2)_m$-, where m= 1-3, X^a is halogen and

$R^7$is as defined in claim 1.

43. **(New)** A method as in claim 42, wherein said substituted cyclic moiety L^1 is phenyl, pyridyl or pyrimidinyl.

44. **(New)** A method of claim 39 wherein L^1 is substituted by $-C(O)R_x$ or $-SO_2R_x$, wherein R_x is NR_aR_b.

45. **(New)** A method of treating a disease mediated by p38 within a host, said method comprising administering to said host a compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L^1)$_q$, where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur other than phenyl,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, $-N(R^7)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m= 1-3, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-NO_2$, $-OR^7$, $-SR^7$ $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, $-CO_2R^7$, $-COR^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NO_2$, $-NR^7R^7$, $-NR^7C(O)R^7$, and $-NR^7C(O)OR^7$; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, $-N(R^7)-$, $-(CH_2)_m$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m= 1-3, X^a is halogen and R^7 is as defined above.

46. **(New)** A method of claim 45 for treating a disease mediated by p38 within a host, said method comprising administering to said host a compound of Formula I :

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L^1)$_q$, where L is a substituted or unsubstituted phenyl or pyridine moiety bound directly to D, L^1 comprises a substituted phenyl or pyrimidinyl moiety, M is a bridging group having at least one atom, q is an integer of from 1-3; and

B is a substituted or unsubstituted pyridine group bound directly to D,

wherein L^1 is substituted by at least one substituent selected from the group consisting of -SO_2R_x, -$C(O)R_x$ and -$C(NR_y)$ R_z,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

-$OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen,

hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, $-N(R^7)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m= 1-3, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-NO_2$, $-OR^7$, $-SR^7$ $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, $-CO_2R^7$, $-COR^7$, -

$C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NO_2$, $-NR^7R^7$, $-NR^7C(O)R^7$, and $-NR^7C(O)OR^7$; with R^7 is as defined above; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, $-N(R^7)-$, $-(CH_2)_m$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m= 1-3, X^a is halogen and R^7 is as defined above.

47. (New) A method of treating a condition mediated by p38 within a host, said method comprising administering to said host a compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-$(M-L^1)_q$, where L is a 5 or 6 membered cyclic structure bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members other than pyridyl, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur other than phenyl,

wherein L^1 is substituted by at least one substituent selected from the group consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)\ R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by

halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN,

$-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, $-N(R^7)-$, $-(CH_2)_m-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a{}_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m= 1-3, and X^a is halogen; and

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-NO_2$, $-OR^7$, $-SR^7$ $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, $-CO_2R^7$, $-COR^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NO_2$, $-NR^7R^7$, $-NR^7C(O)R^7$, and $-NR^7C(O)OR^7$, with R^7 as defined above.

48. (**New**) A method as in claim 47 for the treatment of a disease other than cancer.

49. (**New**) A method as in claim 47 wherein the condition within a host treated by administering a compound of formula I is rheumatoid arthritis, osteoarthritis, septic arthritis, tumor metastasis, periodontal disease, corneal ulceration, proteinuria, coronary thrombosis from atherosclerotic plaque, aneurysmal aortic, birth control, dystrophobic epidermolysis bullosa, degenerative cartilage loss following traumatic joint injury, osteopenias mediated by MMP activity, tempero mandibular joint disease or demyelating disease of the nervous system.

50. **(New)** A method as in claim 47 wherein M is a bridging group which is one or more groups selected from the group consisting of -O-, -S-, -N(R^7)-, -(CH_2)$_m$-, -C(O)-, -CH(OH)-, -(CH_2)$_m$O-, -(CH_2)$_m$S-, -(CH_2)$_m$N(R^7)-, -O(CH_2)$_m$-CHX^a-, -CX^a_2-, -S-(CH_2)$_m$- or -N(R^7)(CH_2)$_m$-, where m= 1-3, X^a is halogen and $R^7$is as defined in claim 1.

51. **(New)** A method as in claim 50, wherein said substituted cyclic moiety L^1 is phenyl or pyrimidinyl.

52. **(New)** A method of claim 47 wherein L^1 is substituted by -C(O)R_x or -SO_2R_x, wherein R_x is NR_aR_b.

53. **(New)** A method of treating a disease mediated by p38 within a host, said method comprising administering to said host a compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L^1)$_q$, where L is a 6 membered aryl moiety or a 6 membered hetaryl moiety bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members other than pyridyl, M is a bridging group having at least one atom, q is an integer of from 1-3; and each cyclic structure of L and L^1 contains 0-4 members of the group consisting of nitrogen, oxygen and sulfur, and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur other than phenyl,

wherein L^1 is substituted by at least one substituent selected from the group

consisting of $-SO_2R_x$, $-C(O)R_x$ and $-C(NR_y)\ R_z$,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

$-OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy,

and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, $-N(R^7)-$, $-(CH_2)_{m}-$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m= 1-3, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-NO_2$, $-OR^7$, $-SR^7$ $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, $-CO_2R^7$, $-COR^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NO_2$, $-NR^7R^7$, $-NR^7C(O)R^7$, and $-NR^7C(O)OR^7$; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, $-N(R^7)-$, $-(CH_2)_m$, -C(O)-, -CH(OH)-, $-(CH_2)_mO-$, $-(CH_2)_mS-$, $-(CH_2)_mN(R^7)-$, $-O(CH_2)_m-$ CHX^a-, $-CX^a_2-$, $-S-(CH_2)_m-$ and $-N(R^7)(CH_2)_m-$, where m= 1-3, X^a is halogen and R^7 is as defined above.

54. **(New)** A method of claim 53 for treating a disease mediated by p38 within a host, said method comprising administering to said host a compound of Formula I :

$$A - D - B \qquad (I)$$

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L^1)$_q$, where L is a substituted or unsubstituted phenyl or pyridine moiety bound directly to D, L^1 comprises a substituted phenyl or pyrimidinyl moiety, M is a bridging group having at least one atom, q is an integer of from 1-3; and

B is a substituted or unsubstituted pyridine group bound directly to D,

wherein L^1 is substituted by at least one substituent selected from the group consisting of -SO_2R_x, -$C(O)R_x$ and -$C(NR_y)$ R_z,

R_y is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally halosubstituted, up to per halo;

R_z is hydrogen or a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

R_x is R_z or NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen, or

-$OSi(R_f)_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and

optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen; or

c) one of R_a or R_b is -C(O)-, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)NR^7R^7$, $-C(O)-R^7$, $-NO_2$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NR^7C(O)OR^7$, $-NR^7C(O)R^7$, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents independently selected from the group consisting of -CN, $-CO_2R^7$, $-C(O)R^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NR^7R^7$, $-NO_2$, $-NR^7C(O)R^7$, $-NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen,

wherein Q is -O-, -S-, $-N(R^7)$-, $-(CH_2)_m$-, -C(O)-, -CH(OH)-, $-(CH_2)_mO$-, $-(CH_2)_mS$-, $-(CH_2)_mN(R^7)$-, $-O(CH_2)_m$- CHX^a-, $-CX^a{}_2$-, $-S-(CH_2)_m$- and $-N(R^7)(CH_2)_m$-, where m= 1-3, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected

from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO_2R^7, -C(O)R^7, -C(O)NR^7R^7, -NO_2, -OR^7, - SR^7 -NR^7R^7, -$NR^7C(O)OR^7$, -$NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO_2R^7, -COR^7, -C(O)NR^7R^7, -OR^7, -SR^7, -NO_2, -NR^7R^7, -$NR^7C(O)R^7$, and -$NR^7C(O)OR^7$; with R^7 is as defined above; and

wherein M is one or more bridging groups selected from the group consisting of -O-, -S-, -$N(R^7)$-, -$(CH_2)_m$, -C(O)-, -CH(OH)-, -$(CH_2)_m$O-, -$(CH_2)_m$S-, -$(CH_2)_m$N(R^7)-, -$O(CH_2)_m$- CHX^a-, -CX^a_2-, -S-$(CH_2)_m$- and -N(R^7)$(CH_2)_m$-, where m= 1-3, X^a is halogen and R^7 is as defined above.

55. (New) A method as in claim 47 wherein the compound of formula I is N-(5-tert-butyl-2-methoxyphenyl)-N'-(4-(4-methoxy-3-(N-methylcarbamoyl)phenoxy)phenyl) urea and its pharmaceutically acceptable salts.

REMARKS

The amendments above serve to delete compounds of formula I recited in the claims such that either L^1 is not pyridyl or B is not phenyl. These amendments have been made to avoid an obviousness type double patenting rejection in copending application 09/889,227.

This divisional application has been filed since the claims are directed to non-elected subject matter of the parent application.

Claims 39-46 and 47-54 correspond to claims 1, 3, 4, 7-11, of the parent application, now abandoned

Applicants elect, in advance, the disease state arthritis and the species recited in claim 55.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

/Richard J. Traverso/

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Date: August 27, 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

William SCOTT et al.

Serial No.: Examiner: Rita J. Desai

Filed: August 27, 2007 Group Art Unit: 1625

Title: ω-CARBOXYARYL SUBSTITUTED DIPHENYL UREAS AS RAF KINEASE INHIBITORS

Preliminary Amendment

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Prior to examination, please amend the above-identified application as follows.

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims, which begins on page 3 of this paper.

Remarks/Arguments begin on page 13 of this paper.

In the Specification:

On page 1, please amend the first full paragraph as follows:

~~This is a continuation-in-part of Serial No. 09/257,266 filed February 25, 1999 and a continuation-in-part of Serial No. 60/115,877 filed January 13, 1999.~~

This is a division of Application No. 09/948,915, filed September 10, 2001, which is a continuation of Application No. 09/425,228, filed October 22, 1999, which is a continuation-in-part of Serial No. 09/257,266 filed February 25, 1999 which claims the benefit of the filing date of U.S. provisional application Serial No. 60/115,877 filed January 13, 1999. The content of these applications are incorporated herein by reference.

This listing of claims will replace all prior versions, and listings, of claims in the application:

LISTING OF CLAIMS:

1. - 67 (Cancelled)

68. (New) A compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: -L-(M-L^1)$_q$, where L is a 6 membered aryl moiety which is unsubstituted phenyl bound directly to D, L^1 comprises a substituted cyclic moiety having at least 5 members which is phenyl pyridyl, M is -O- and

B is a substituted or unsubstituted, up to tricyclic aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 6-member cyclic structure bound directly to D which is pyridinyl

wherein L^1 is substituted by -C(O)R_x

R_x is NR_aR_b where R_a and R_b are

a) independently hydrogen,

a carbon based moiety of up to 30 carbon atoms optionally containing heteroatoms selected from N, S and O, which is of C_1 -C_{10} alkyl, C_1-C_{10} alkoxy, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_{3-12} hetaryl having 1-3 heteroatoms selected from O, N and S, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl or C_7-C_{24} alkaryl, and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O, which are C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6-C_{12} halo substituted aryl up to per halo aryl, C_3-C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3-C_{12} hetaryl up to per halo hetaryl, halo substituted C_7-C_{24} aralkyl up to per halo aralkyl, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, or -C(O)R_g or

-OSi(R_f)$_3$ where R_f is hydrogen or a carbon based moiety of up to 24 carbon atoms optionally containing heteroatoms selected from N, S and O and optionally substituted by halogen, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O, which are C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_7 -C_{24} alkaryl, C_7 -C_{24} aralkyl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6-C_{12} halo substituted aryl up to per halo aryl, C_3-C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3-C_{12} hetaryl up to per halo hetaryl, halo substituted C_7-C_{24} aralkyl up to per halo aralkyl, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, or -C(O)R_g, or

b) R_a and R_b together form a 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O, or a substituted 5-7 member heterocyclic structure of 1-3 heteroatoms selected from N, S and O substituted by halogen, hydroxy or carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O, which are C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_7 -C_{24} alkaryl, C_7 -C_{24} aralkyl, halo substituted C_{1-6} alkyl up to per halo alkyl, halo substituted C_6-C_{12} aryl up to per halo aryl, halo substituted C_3-C_{12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3-C_{12} hetaryl up to per halo hetaryl, halo substituted C_7-C_{24} aralkyl up to per halo aralkyl, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, or -C(O)R_g, or

c) one of R_a or R_b is -C(O)-, a C_1-C_5 divalent alkylene group or a substituted C_1-C_5 divalent alkylene group bound to the moiety L to form a cyclic structure with at least 5 members, wherein the substituents of the substituted C_1-C_5 divalent alkylene group are selected from the group consisting of halogen, hydroxy, and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O, which are C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_7 -C_{24} alkaryl, C_7 -C_{24} aralkyl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6-C_{12} halo substituted aryl up to per halo aryl, C_3-C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo substituted C_3-C_{12} hetaryl up to per

halo hetaryl, halo substituted C_7-C_{24} aralkyl up to per halo aralkyl, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, or -C(O)R_g, and are optionally substituted by halogen;

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO_2R^7, -C(O)NR^7R^7, -C(O)-R^7, -NO_2, -OR^7, -SR^7, -NR^7R^7, -$NR^7C(O)OR^7$, -$NR^7C(O)R^7$, -Q-Ar, and carbon based moieties of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O, which are C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_7 -C_{24} aralkyl, or C_3-C_{12} heteroaryl having 1-3 heteroatoms selected from O, N and S, and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO_2R^7, -C(O)R^7, -C(O)NR^7R^7, -OR^7, -SR^7, -NR^7R^7, -NO_2, -$NR^7C(O)R^7$, -$NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O, which are C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_3-C_{13} hetaryl having 1-3 heteroatoms selected from O, N and S, C_7-C_{14} alkaryl, C_7-C_{24} aralkyl, C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and optionally substituted by halogen,

wherein Q is -O-, -S-, -N(R^7)-, -$(CH_2)_m$-, -C(O)-, -CH(OH)-, -$(CH_2)_m$O-, -$(CH_2)_m$S-, -$(CH_2)_m$N(R^7)-, -O$(CH_2)_m$- CHX^a-, -CX^a_2-, -S-$(CH_2)_m$- and -N(R^7)$(CH_2)_m$-, where m= 1-3, and X^a is halogen;

Ar is a 5- or 6-member aromatic structure containing 0-2 members selected from the group consisting of nitrogen, oxygen and sulfur, which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO_2R^7, -C(O)R^7, -C(O)NR^7R^7, -NO_2, -OR^7, - SR^7 -NR^7R^7, -$NR^7C(O)OR^7$, -$NR^7C(O)R^7$, and a carbon based moiety of up to 24 carbon atoms, optionally containing heteroatoms selected from N, S and O, which is C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_6-C_{14} aryl, C_3-C_{13} hetaryl having 1-3 heteroatoms selected from O, N and S, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, C_4-C_{23} alkheteroaryl having 1-3

heteroatoms selected from O, N and S, and optionally substituted by one or more substituents are selected from the group consisting of -CN, $-CO_2R^7$, $-COR^7$, $-C(O)NR^7R^7$, $-OR^7$, $-SR^7$, $-NO_2$, $-NR^7R^7$, $-NR^7C(O)R^7$, and $-NR^7C(O)OR^7$, with R^7 as defined above; and where R_g is C_{1-10} alkyl; -CN, $-CO_2R_d$, $-OR_d$, $-SR_d$, $-NO_2$, $-C(O)R_e$, $-NR_dR_e$, $-NR_d C(O)OR_e$ and $-NR_d C(O)R_e$, and R_d and R_e are independently selected from the group consisting of hydrogen, C_{1-10}, alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_{6-12} aryl, C_3-C_{12} hetaryl with 1-3 heteroatoms selected from O, N and S and C_7-C_{24} aralkyl, C_7 -C_{24} alkaryl, up to per halo substituted C_1-C_{10} alkyl, up to per halo substituted C_3 -C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted C_6 -C_{14} aryl, up to per halo substituted C_3 -C_{12} hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, or up to per halo substituted C_7-C_{24} aralkyl.

69. **(New)** A compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of up to 40 carbon atoms of the formula: $-L-(M-L^1)_q$, where L is a substituted or unsubstituted phenyl or pyridinyl moiety bound directly to D, L^1 comprises a substituted phenyl moiety, M is -O- and

B is a substituted or unsubstituted phenyl group bound directly to D,

wherein L^1 is substituted by $-C(O)R_x$,

R_x is NR_aR_b where R_a and R_b are

a) independently hydrogen,

a moiety, which is C_1 -C_{10} alkyl, C_1-C_{10} alkoxy, C_{3-10} cycloalkyl, C_{2-10} alkenyl, C_{1-10} alkenoyl, C_{6-12} aryl, C_{3-12} hetaryl having 1-3 heteroatoms selected from O, N and S, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from N, S and O, C_{7-24} aralkyl, or C_7-C_{24} alkaryl, and optionally substituted by halogen, hydroxy and carbon based substituents which are C_{1-10} alkyl, C_{3-12} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_{3-12} hetaryl having 1-3 heteroatoms selected from N, S and O, C_{1-10} alkoxy, C_{6-12} aryl, C_{1-6} halo substituted alkyl up to per halo alkyl, C_6-C_{12} halo substituted aryl up to per halo aryl, C_3-C_{12} halo substituted cycloalkyl having 0-3 heteroatoms selected from N, S and O, up to per halo cycloalkyl, halo

substituted C_3-C_{12} hetaryl up to per halo hetaryl, halo substituted C_7-C_{24} aralkyl up to per halo aralkyl, or halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, and -C(O)R_g,

where B is substituted, L is substituted or L^1 is additionally substituted, the substituents are selected from the group consisting of halogen, up to per-halo, and Wn, where n is 0-3;

wherein each W is independently selected from the group consisting of -CN, -CO_2R^7, -C(O)NR^7R^7, -C(O)-R^7, -NO_2, -OR^7, -SR^7, -NR^7R^7, -$NR^7C(O)OR^7$, -$NR^7C(O)R^7$, -Q-Ar, and moieties which are C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, C_3-C_{12} heteroaryl having 1-3 heteroatoms selected from O, N and S, or C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and optionally substituted by one or more substituents independently selected from the group consisting of -CN, -CO_2R^7, -C(O)R^7, -C(O)NR^7R^7, -OR^7, -SR^7, -NR^7R^7, -NO_2, -$NR^7C(O)R^7$, -$NR^7C(O)OR^7$ and halogen up to per-halo; with each R^7 independently selected from H or a moiety which is C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, S and N, C_6-C_{14} aryl, C_3-C_{13} hetaryl having 1-3 heteroatoms selected from O, N and S, C_7-C_{14} alkaryl, C_7-C_{24} aralkyl, or C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S,

wherein Q is -O-, -S-, -N(R^7)-, -$(CH_2)_m$-, -C(O)-, -CH(OH)-, -$(CH_2)_m$O-, -$(CH_2)_m$S-, -$(CH_2)_m$N(R^7)-, -O$(CH_2)_m$- CHX^a-, -CX^a_2-, -S-$(CH_2)_m$- and -N(R^7)$(CH_2)_m$-, where m= 1-3, and X^a is halogen;

Ar is phenyl or pyridinyl which is optionally substituted by halogen, up to per-halo, and optionally substituted by Z_{n1}, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO_2R^7, -C(O)R^7, -C(O)NR^7R^7, -NO_2, -OR^7, -SR^7 -NR^7R^7, -$NR^7C(O)OR^7$, -$NR^7C(O)R^7$, and a moiety which is C_1-C_{10} alkyl, C_1-C_{10} alkoxy, C_2-C_{10} alkenyl, C_1-C_{10} alkenoyl, C_3-C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_6-C_{14} aryl, C_3-C_{13} hetaryl having 1-3 heteroatoms selected from O, N and S, C_7-C_{24} alkaryl, C_7-C_{24} aralkyl, or C_4-C_{23} alkheteroaryl having 1-3 heteroatoms selected from O, N and S, and optionally substituted by one or more substituents selected from the group consisting of -CN, -CO_2R^7, -COR^7, -C(O)NR^7R^7, -OR^7, -SR^7, -NO_2, -NR^7R^7, -$NR^7C(O)R^7$, and -$NR^7C(O)OR^7$; and where R_g is $C_{1\text{-}10}$ alkyl; -CN, -CO_2R_d, -OR_d, -SR_d, -NO_2, -C(O)R_e, -NR_dR_e, -NR_d C(O)OR_e and -NR_d C(O)R_e, and R_d and R_e are independently selected from the

group consisting of hydrogen, C_{1-10}, alkyl, C_{1-10} alkoxy, C_{3-10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, C_{6-12} aryl, C_3-C_{12} hetaryl with 1-3 heteroatoms selected from O, N and S and C_7-C_{24} aralkyl, C_7 -C_{24} alkaryl, up to per halo substituted C_1-C_{10} alkyl, up to per halo substituted C_3 -C_{10} cycloalkyl having 0-3 heteroatoms selected from O, N and S, up to per halo substituted C_6 -C_{14} aryl, up to per halo substituted C_3 -C_{12} hetaryl having 1-3 heteroatoms selected from O, N, and S, halo substituted C_7-C_{24} alkaryl up to per halo alkaryl, or up to per halo substituted C_7-C_{24} aralkyl.

70. **(New)** A compound as in claim 68 wherein the cyclic structures of B and L bound directly to D have hydrogen substituents in the ortho position.

71. **(New)** A compound as in claim 69 wherein the cyclic structures of B and L bound directly to D have hydrogen substituents in the ortho position.

72. **(New)** A compound as in claim 68 wherein substituents for B and L and additional substituents for L^1, are selected from the group consisting of C_1-C_{10} alkyl up to per halo substituted C_1-C_{10} alkyl, CN, OH, halogen, C_1-C_{10} alkoxy and up to per halo substituted C_1-C_{10} alkoxy.

73. **(New)** A compound as in claim 69 wherein substituents for B and L and additional substituents for L^1, are selected from the group consisting of C_1-C_{10} alkyl up to per halo substituted C_1-C_{10} alkyl, CN, OH, halogen, C_1-C_{10} alkoxy and up to per halo substituted C_1-C_{10} alkoxy.

74. **(New)** A compound of claim 68 wherein R_a and R_b are independently hydrogen and C_{1-6} alkyl .

75. **(New)** A compound of claim 69 wherein R_a and R_b are independently hydrogen and C_{1-6} alkyl, hydroxy and carbon based substituents of up to 24 carbon atoms, which optionally contain heteroatoms selected from N, S and O and are optionally substituted by halogen.

76. **(New)** A pharmaceutically acceptable salt of a compound of claim 68 which is

a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

77. **(New)** A pharmaceutically acceptable salt of a compound of claim 69 which is

a) a basic salt of an organic acid or inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

78. **(New)** A pharmaceutical composition comprising a compound of claim 68 and a physiologically acceptable carrier.

79. **(New)** A pharmaceutical composition comprising a compound of claim 69 and a physiologically acceptable carrier.

80. **(New)** A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of claim 68.

81. **(New)** A method for the treatment of a cancerous cell growth mediated by raf kinase, comprising administering a compound of claim 69.

82. **(New)** A compound of Formula I:

A - D - B (I)

or a pharmaceutically acceptable salt thereof, wherein

D is -NH-C(O)-NH-,

A is a substituted moiety of the formula:

-L-M-L^1,

wherein L is

phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, C_1-C_5 linear or branched haloalkyl up to perhalo, C_1-C_3 alkoxy, C_1-C_3 haloalkoxy up to per haloalkoxy, hydroxy, amino, C_1-C_3 alkylamino, C_1-C_6 dialkylamino, halogen, cyano, and nitro;

L^1 comprises a substituted cyclic moiety which is

phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R^7, OR^7, $NR^7R^{7'}$, $C(O)R^7$, $C(O)OR^7$, $C(O)NR^7R^{7'}$, $NR^7C(O)R^{7'}$, $NR^7C(O)OR^{7'}$, halogen, cyano and nitro;

and

wherein R_x is R_z or NR_aR_b and R_a and R_b are, independently, R_z

M is -O-

B is

(i) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of R^7, OR^7, $NR^7R^{7'}$, $C(O)R^7$, $C(O)OR^7$, $C(O)NR^7R^{7'}$, $NR^7C(O)R^{7'}$, $NR^7C(O)OR^{7'}$ halogen, cyano, and nitro; or

(ii) pyridinyl optionally substituted with 1-3 substituents independently selected from the group consisting of R^7, OR^7, $NR^7R^{7'}$, $C(O)R^7$, $C(O)OR^7$, $C(O)NR^7R^{7'}$, $NR^7C(O)R^{7'}$, $NR^7C(O)OR^{7'}$, halogen, cyano, and nitro; and

each R^7, $R^{7'}$, R_z and R_f is independently

(a) hydrogen,

(b) C_1-C_6 linear, branched, or cyclic alkyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy and hydroxy;

(c) C_1-C_6 alkoxy, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy, hydroxy and halogen;

(d) phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy, hydroxy and halogen,

(e) 5-6 membered monocyclic heteroaryl having 1-4 heteroatoms selected from the group consisting of O, N and S or 8-10 membered bicyclic heteroaryl having 1-6 heteroatoms selected from the group consisting of O, N and S, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy, hydroxy and halogen,

(f) C_1-C_3 alkyl-phenyl, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy, hydroxy and halogen; and

(g) up to per–halo substituted C_1-C_5 linear, branched or cyclic alkyl, and where not per-halo substituted, optionally substituted with 1-3 substituents independently selected from the group consisting of C_1-C_5 linear or branched alkyl, up to perhalo substituted C_1-C_5 linear or branched alkyl, C_1-C_3 alkoxy and hydroxy.

83. **(New)** A compound of claim 82 wherein the substituents of the substituted structures of L are selected from the group consisting of methyl, triflouromethyl, ethyl, n-propyl, n-butyl, n-pentyl, i-propyl, t-butyl, methoxy, ethoxy, propoxy, Cl, Br, F, cyano, nitro, hydroxy, amino, methylamino, dimethylamino, ethylamino and diethylamino.

84. **(New)** A compound of claim 82 wherein the substituents of the substituted structures of B and L^1 are independently selected from the group consisting of methyl, triflouromethyl, ethyl, n-propyl, n-butyl, n-pentyl, isopropyl, tert-butyl, sec-butyl, isobutyl,

cyclopropyl, cyclobutyl, cyclopentyl, methoxy, ethoxy, propoxy, Cl, Br and F, cyano, nitro, hydroxy, amino, methylamino, dimethylamino, ethylamino and diethylamino.

85. **(New)** A compound as in claim 82 wherein B, L and L^1 follow one of the following of combinations:

B= phenyl, L=phenyl and L^1 is phenyl,

B=pyridinyl, L= phenyl and L^1 is phenyl,

B=pyridinyl, L=phenyl and L^1 is pyridinyl,

86. **(New)** A pharmaceutical composition for the treatment of a cancerous cell growth comprising a compound of claim 82 or a pharmaceutically acceptable salt of a compound of formula I and a physiologically acceptable carrier.

87. **(New)** A pharmaceutical composition for the treatment of a cancerous cell growth as in claim 86 wherein the pharmaceutically acceptable salt is

a) a basic salt of an organic acid or an inorganic acid which is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulfonic acid, trifluoromethanesulfonic acid, benzenesulfonic acid, p-toluene sulfonic acid (tosylate salt), 1-napthalene sulfonic acid, 2-napthalene sulfonic acid, acetic acid, trifluoroacetic acid, malic acid, tartaric acid, citric acid, lactic acid, oxalic acid, succinic acid, fumaric acid, maleic acid, benzoic acid, salicylic acid, phenylacetic acid, or mandelic acid; or

b) an acid salt of an organic or inorganic base containing an alkali metal cation, an alkaline earth metal cation, an ammonium cation, an aliphatic substituted ammonium cation or an aromatic substituted ammonium cation.

REMARKS

The above amendment directs the claims to compounds of formula I

A - D - B (I)

salts thereof, compositions which contain them and methods for using them, wherein either

- A is of the formula: -L-(M-L^1)$_q$, and L^1 is phenyl; and/or
- "B" is phenyl.

This amendment is made for the purposes of 1) avoiding an obviousness type double patenting rejection in related copending Application No. 09/889,227 and 2) directing the claims in this divisional application to subject matter which was not elected in the parent application.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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Date: August 27, 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Confirmation No.: 3172

RIEDL, Bernd, et. al. Examiner: Delacroix Muirhei, Cybille

Serial No.: 10/086,417 Group Art Unit: 1614

Filed: March 4, 2002

Title: OMEGA-CARBOXY ARYL SUBSTITUTED DIPHENYL UREAS AS p38 KINASE INHIBITORS

EXPRESS ABANDONMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants abandon this application without disclaiming the subject matter defined and claimed herein and without prejudice to pursuing this subject matter in divisional application serial no. 11/845,597, filed August 27, 2007.

Respectfully submitted,

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Filed: August 28, 2007

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Khire Uday		Confirmation No. 9834	
Serial No.:	09/948,915	Examiner:	Rita J. Desai
Filed:	September 10, 2001	Group Art Unit:	1625

Title: ω-CARBOXYARYL SUBSTITUTED DIPHENYL UREAS AS RAF KINEASE INHIBITORS

EXPRESS ABANDONMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants abandon this application without disclaiming the subject matter defined and claimed herein and without prejudice to pursuing this subject matter in divisional application serial no. 11/845,595, filed August 27, 2007.

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Filed: August 28, 2007